DOES CHRONIC VENOUS INSUFFICIENCY PLAY A ROLE IN MS PATHOGENESIS? "NO"

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Daclizumab is part of an expanding class of new drugs with monospecifi c modes of action that are being evaluated for the treatment of patients with multiple sclerosis. Like many of these treatments, daclizumab is the result of rational drug design.

Daclizumab is a recombinant humanised monoclonal antibody that was engineered to bind to the α subunit of the high-affinity interleukin-2 receptor (CD25). CD25 is a type I transmembrane protein that is expressed on the surface of numerous cell types, including thymocytes, myeloid precursor cells, and activated T lymphocytes and B lymphocytes. In association with CD122, CD25 forms a heterodimer that can act as a high-affinity receptor for interleukin 2.

In a recent phase II clinical trial, 230 patients were randomly assigned to receive interferon beta and high-dose daclizumab, interferon beta and low-dose daclizumab, or interferon beta and placebo. The adjusted mean number of new or enlarged gadolinium contrast-enhancing lesions was 4·75 in the interferon beta and placebo group compared with 1·32 in the interferon beta and high-dose daclizumab group (difference 72%, 95% CI 34% to 88%; p=0·004) and 3·58 in the interferon beta and low-dose daclizumab group (25%, −76% to 68%; p=0·51). In the pharmacodynamic substudy, daclizumab was not associated with significant changes in absolute numbers of T cells, B cells, or natural killer cells, or T-cell proliferative response compared with interferon beta alone. The number of CD56bright natural killer cells was seven to eight times higher in both daclizumab groups than in the interferon beta and placebo group (interferon beta and low-dose daclizumab group p=0·002; interferon beta and high-dose daclizumab group p<0·0001). Common adverse events were equally distributed across groups.

Add-on daclizumab treatment reduced the number of new or enlarged gadolinium contrast-enhancing lesions compared with interferon beta alone and might reduce multiple sclerosis disease activity to a greater extent than interferon beta alone.